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THE PRINCIPLE OF VENOUS PRESSURE REDUCTION IN THE TREATMENT OF HEART FAILURE

I. *Venous Pressure and Heart Failure*

The remarkable relief which is given by venesection in the treatment of certain cases of congestive cardiac failure is well known. It is only in recent years, however, that further study of the mechanism of this relief by cardiac catheterization has slightly clarified the rationale of this procedure. Depression of cardiac output is not an essential part of the progress of development of cardiac failure[1, 4, 9]. Venous congestion is therefore no longer regarded as the result of failure of the heart to pass blood into the arterial system but rather the consequence of various reflex and other adaptations of venous pressure, initiated for the maintenance of cardiac output.

The output of the *isolated* heart is largely determined by the length of the myocardial fibres in diastole. The greater the diastolic volume of the heart, the greater the stroke output (Starling). The length of the myocardial fibres in diastole is determined mainly by the pressure under which the ventricle is filled (diastolic tension) and this, in turn, depends upon the pressure in the right atrium and central veins. There is a close linear relationship between the venous filling pressure and the cardiac output in the isolated normal heart.

Starling, however, established a further important point. If he went on raising the venous filling pressure of the isolated heart beyond a certain optimum point the output would no longer rise, and if the pressure was raised still further the output of the heart would begin to fall. Increasing venous filling pressure therefore only increases the output of the heart within certain physiological limits. Beyond those limits the heart is over-stretched, further increase in output is not possible and by increasing the stretching still further the output may, in fact, decline. In Fig. I these relationships are shown and the falling part of the curve may be described as the *reaction of the overloaded heart.*

II. *Evidence of Overloading of the Human Heart in Failure and the Response to Venesection*

The common forms of heart failure resulting from valvular, ischemic, and hypertensive heart disease present in their terminal stages a hemodynamic picture of grossly raised venous pressure and low cardiac output. We have named this group the low output group. At this stage there is evidence that the heart behaves as though it were on the overloaded part of the Starling curve. The evidence is as follows:

1. Acute exacerbations of cardiac failure are likely to develop in the recumbent position. In this position the venous pressure in the neighborhood of the right heart is increased so that the heart is put under a greater stretching influence. After a time acute left ventricular failure develops with paroxysmal nocturnal orthopnea (cardiac asthma).

2. The relief which is given in this condition by adopting the upright position is well known. In this position the hydrostatic pressure in the great veins near the heart is reduced.

3. Attempts to take exercise are accompanied in such patients by a rise in venous pressure but the cardiac output may actually decline[3].

4. Infusions and transfusions which raise the venous pressure may precipitate cardiac failure in such patients[12].

5. Venesection induces a fall in venous pressure which is commonly accompanied by a rise in cardiac output[3].

III. *The Action of Mercurial Diuretics*

It is well known that mercurial diuretics depress the reabsorption of water and salt by the renal tubules causing elimination of large quantities of edema fluid. If this were its only action, the use of mercurials in cardiac failure would be purely symptomatic treatment. Pugh and Wyndham[11] have demonstrated that, during the few hours following the injection of sodium mersalylate, the venous pressure falls considerably and accompanying this there is often a rise in cardiac output. There is no pharmacological evidence that mercurials have any direct stimulating action on the myocardium and the most probable explanation of this action is a "venesec-

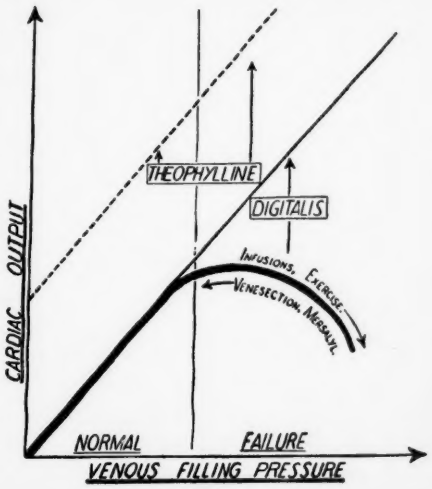

FIG. I

The thick line represents the "Starling curve." The influence of venous pressure change in heart failure is shown. Digitalis increases the output of the failing heart only, theophylline increases the output of the normal and the failing heart.

tion-like" influence of the mercurials through blood volume reduction. During the elimination of protein free filtrate from plasma accompanying the diuresis there is some hemoconcentration and this may represent quite a significant reduction of the blood volume, which, in turn, may determine a fall in venous and right atrial pressure. The overloaded overstretched heart may thereby recover some of its tone with a corresponding improvement in cardiac output.

IV. *Cardiotonic Drugs*

(a) *Theophylline.* When given intravenously to patients with hypertensive cardiac failure theophylline has a conspicuous action in reducing the venous pressure and increasing the cardiac output[4]. This action comes on within a few minutes, and in hypertensive failure this immediate action is quantitatively much greater than any comparable immediate action of digoxin. The output of the heart after theophylline was always much greater than could be accounted for by venous pressure reduction, and, in contrast to digitalis, theophylline increases the output of the normal heart. Such observations made it clear that theophylline has a direct stimulating action on the heart and that the venous pressure reduction was probably a secondary consequence of cardiac output improvement. While theophylline has a marked stimulating action on the heart it should be remembered that this action is very transient, often lasting less than half an hour. Its action is less pronounced in mitral stenosis than in hypertension and ischemic heart disease. Stimulation of the heart may be dangerous in myocardial infarction where theophylline is given for its alleged vasodilator action on the coronary arteries. There are great difficulties in giving this drug effectively by any route other than intravenous injection. It causes digestive disturbances when given orally.

(b) *Digitalis.* In the normal heart digitalis either has no influence on, or reduces cardiac output. Digitalis reduces the venous pressure and usually increases the cardiac output in patients with low output failure. In many cases, however, digoxin reduces the venous pressure without altering the output of the heart significantly. This led to the suggestion that digitalis might have primary action reducing venous tone and that its effect on the output of the heart might result from venous pressure reduction[5]. The response of the heart output might be determined by its relation to the Starling curve: an increase if the heart was overloaded, no change or a fall if it was on the summit of the curve.

More recently, however, we have realized that there may be another explanation for venous pressure fall in the absence of cardiac output change[7]. In left ventricular failure the pulmonary artery systolic pressure may rise to 60 or 70 mm. Hg. or more from a normal value of 18—30 mm. Hg. The very high pulmonary arterial pressure seems to be a secondary consequence of a considerable rise in pulmonary venous pressure in such patients. We have observed that digoxin may reduce this raised pulmonary vascular pressure in left ventricular failure to a nearly normal level without measurable change in the cardiac output. It is possible to explain these actions by postulating that the failing left ventricle is enabled by digitalis to maintain the same output with a lower filling pressure in the pulmonary veins[10]. Before the pulmonary venous pressure falls the output of the left ventricle for a few beats increases slightly above that of the right. Such a small temporary difference (not susceptible to measment by the methods now in use) quickly leads to a fall in pulmonary venous pressure, whereupon the outputs of the two ventricles are equalized. The fall in pulmonary venous pressure leads to reduction of the raised pulmonary arterial pressure. Relief of the load of pulmonary hypertension on the right ventricle in turn produces a fall in the filling pressure of this chamber and hence a fall in systemic venous pressure. Differential digitalis stimulation of a failing left ventricle may thus account for a fall in systemic venous pressure without more than a very transient initial increase in cardiac output, which settles back to the control level after a few beats. Previously emphasized similarity between the effects of digitalis and venesection on cardiac output may simply be represented as arrival at the same point on a Starling curve by different routes (Fig. I).

Reduction of pulmonary vascular congestion, however, gives considerable symptomatic relief of dyspnea in heart failure whether accompanied by an increase in cardiac output or not. Reduction in pressure in the lung vessels is an important index of successful therapy in left ventricular failure. Often, with digoxin, the cardiac output improves a few minutes after pressure reduction, but sometimes cardiac output improvement is slowly progressive over several hours or even days.

Relief of congestion and cardiac output improvement are quite as effective following digitalization in patients with sinus rhythm as in patients with auricular fibrillation. The pronounced rate reduction in the latter condition seems to contribute little to the clinical response[6].

V. *The High Output Group*

The remarks made above apply to patients with hypertensive, ischemic, and valvular heart disease, in whom the output tends to fall to a low level in the advanced stages of cardiac failure. There is another group of patients in whom the output of the heart in failure tends to be high. To this group belong patients with severe anemia and with emphysema. In such subjects the oxygen carrying power of the blood is diminished, a high cardiac output being necessary for the maintenance of oxygenation of the tissues. All the phenomena of cardiac failure with edema and venous congestion may make their appearance with cardiac output values which are above the normal average level. In such patients the raised venous pressure is probably part of a compensating mechanism. Many of these patients have not reached the overloading part of the Starling curve and reduction of filling pressure by venesection may lead to a fall in the cardiac output with no satisfactory clinical improvement or possibly even deterioration. Venesection is therefore likely to be of little value in patients with emphysema heart failure. Curiously enough digitalis is also less likely to be of benefit in such patients. There is very definite parallelism between the cardiac output improvement with digitalization and a similar beneficial response to venesection. It is the overloaded heart which responds well to both remedies. So long as the heart is making a normal type of response to venous pressure change, venesection is likely to diminish the output of the heart and digitalis is likely either to be without effect or even to reduce the output of the heart.

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